REMARKS

By this amendment, claims 1, 6, 7 are amended, claim 14 is canceled without prejudice or disclaimer. These amendments are made to even more clearly recite the claimed invention, do not add prohibited new matter and are fully supported by the specification. Reconsideration and withdrawal of the rejections in the outstanding Office Action are respectfully requested in view of the foregoing amendments and the following remarks.

Claim Rejections – 35 U.S.C. § 112, second paragraph

The Office Action rejects claim 14 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Examiner asserts that the recitation "goodness of fit" lacks proper antecedent basis. Without agreeing with or acquiescing to the rejection, Applicants note that claim 14 has been canceled. Applicants respectfully request withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 101

The Office Action asserts that claims 1, 6, 7, and 11, and 14 are directed to non-statutory subject matter, alleging that the claims do not recite a physical transformation of matter. Specifically, the Examiner asserts that the recitation "readily accessible memory" or a "computer on a network" is not tangible media. Without agreeing with or acquiescing to the rejection, Applicants note that the claims have been amended to remove the reference to the allegedly non-statutory subject matter. Applicants respectfully request withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 102

The Office Action rejects claims 1, 6, 7, and 11-13 under 35 U.S.C. 102(b) as being anticipated by Wang et al. (J. Med. Chem., Vol. 37, pp. 4479-4489 (1994), hereinafter "WANG"). In response, Applicants respectfully submit that WANG does not anticipate the claimed invention.

WANG is directed to a method for finding compounds that bind to protein kinase C (PK-C). WANG acknowledges that "the 3D structure of the PK-C receptor has not yet been determined" (*see* page 4480, col. 1, paragraph 2, of WANG). Therefore, WANG relies on information on the pharmacophore of PDBU (phorbol 12, 13-dibutyrate), which is known to bind to PK-C ("protein kinase C") (*see* page 4480, col. 1, paragraph 2, of WANG). Based on the crystal structure of the phorbol ester and information on binding sites of PDBU, WANG constructed a 3D pharmacophore query for PDBU (*see* page 4480, col. 1, paragraph 3, of WANG). However, this pharmacophore query did not include information on the binding sites or three-dimensional structure of the PK-C protein; the search relied solely on information on the pharmacophore structure of PDBU. The pharmacophore search retrieved 535 compounds, and samples were available for only 286 compounds out of the 535 compounds. The structures of the 286 compounds were then visually inspected, and 161 compounds were excluded based upon the visual inspection. Then, the binding affinity of the remaining 125 compounds was evaluated by means of a PK-C bioassay (*see* page 4480, col. 2, paragraph 4, of WANG).

In contrast, claim 1 recites "estimating a binding scheme of the lead-candidate compounds to the protein based on three-dimensional information of the query molecule, binding scheme of the query molecule to the protein, and correspondence of the mode of covalent bonds of the partial structures of the query molecule and the trial compounds." Again, the pharmacophore query in

WANG does not actually use the "three-dimensional information" of PDBU, the known ligand for PK-C. Rather, the pharmacophore query disclosed in WANG relies primarily upon known distances between *three* oxygen atoms in the phorbol ester, which fails to bind to PK-C (as acknowledged on page 4480, col. 1, paragraph 2, of WANG; *see* Figure 1 of WANG). In addition, the pharmacophore query in WANG generally requires the existence of hydrophobic hydroxyl functional group information on the binding sites of a known ligand (i.e., PDBU).

WANG does not "estimate[e] a binding scheme of the lead-candidate compounds to the protein *based on three-dimensional information of the query molecule*," as recited in the claims. Instead, the pharmacophore query in WANG merely relies upon three distances between oxygen atoms from the structure of a molecule (the phorbol ester) that does not even bind to the target protein (PK-C), and generally requires a hydrophobic hydroxyl group. Applicants further submit that the general requirements of the pharmacophore search in WANG would not enable one skilled in the art to "estimate[e] a binding scheme of the lead-candidate compounds to the protein *based on three-dimensional information of the query molecule*," as recited in the claims. This conclusion is supported by the fact that the search method in WANG relies ultimately upon a PK-C bioassay because the broad scope of the pharmacophore search in WANG yields a large number of search results.

Furthermore, as noted above, WANG acknowledges that "the 3D structure of the PK-C receptor has not yet been determined," which further demonstrates that teachings of WANG do not include "estimating...[the] binding scheme of the query molecule to the protein," as recited in the claims (*see* page 4480, col. 1, paragraph 2, of WANG). For at least these reasons, Applicants respectfully submit that WANG fails to teach each and every element of the claimed invention, as

required under 35 U.S.C. § 102(b). Applicants respectfully submit that WANG does not anticipate the claimed invention, and request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, it is submitted that the Examiner's rejections should be withdrawn. Entry and consideration of the present amendment, reconsideration of the outstanding Office Action, and allowance of the present application and all of the claims therein are respectfully requested and now believed to be appropriate.

Any amendments to the claims which have been made in this amendment, and which have not been specifically noted to overcome a rejection based upon the prior art, should be considered to have been made for a purpose unrelated to patentability, and no estoppel should be deemed to attach thereto.

Should the Commissioner determine that any extension of time is required in order to render this response timely and/or complete, a formal request for an extension of time, under 37 C.F.R. §1.136(a), is herewith made in an amount equal to the time period required to render this response timely and/or complete. The Commissioner is authorized to charge any required extension of time fee under 37 C.F.R. §1.17 to Deposit Account No. 19-0089.

If the Examiner has any questions, or wishes to discuss this matter, the Examiner is respectfully requested to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
A. ITAI et al.

Bruce H. Bernstein
Reg. No. 29,027 42,920

June 22, 2008
GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke
Reston, VA 20191
(703) 716-1191